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Roche



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OCT O 6 2006

Tamiflu readily available for 2006/2007 influenza season

Production expansion ensures supply for both seasonal use and pandemic stockpiling

Roche announces that its antiviral medication Tamiflu (oseltamivir) is readily available for the forthcoming 2006-2007 influenza season for the treatment and prevention of influenza. Seasonal influenza is a debilitating and disruptive illness that affects millions of people each year and can lead to complications and death if not treated. Roche can also confirm that any government and corporate orders for stockpiling for an influenza pandemic are being progressed.

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"During the past year, Roche has been gearing up its production capacity and we will be in a position to produce 400 million treatment courses by the end of this year", said William M. Burns, CEO Division Roche Pharma. "Physicians can be confident that Tamiflu will be readily and widely available to patients who need it this season for flu treatment and post-exposure prevention. The measures taken also enable us to schedule any additional orders from governments and corporations who are stockpiling Tamiflu in preparation for an influenza pandemic. Of course, the rate at which this capacity is utilized will depend in large part on the future order flow and the severity of this year's influenza season".

During the 2005 -2006 season Roche had to restrict distribution of Tamiflu to wholesalers in many markets to ensure availability during an influenza outbreak, whilst the production capacity was being expanded. This led to the perception that Tamiflu was in short supply. Based on the available manufacturing capacities, the supply shortage no longer exits.

## Manufacturing Capacity

The broad availability of Tamiflu for both seasonal and pandemic use is due to expanded global production capacity, which will reach the rate of 400 million treatment courses annually by the end of 2006, a more than 10-fold increase since 2004. Roche's global network for the manufacture

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Fex 081 - 689 27 75 http://www.rocha.com of Tamiflu includes several Roche sites and more than 15 external contractors located in 10 different countries around the world. The expansion includes a fully functioning European supply chain and a North American supply chain for Tamiflu with an annual capacity of 80 million treatment courses. In addition, Roche has further extended global availability by offering sublicenses to Hetero Pharmaceuticals and the HEC Group in India and Shanghai Pharmaceuticals in China. Roche has also finalised an agreement on sharing technical know-how with the South African company Aspen, allowing them to supply for pandemic use in the African continent.

#### About influenza

Influenza, commonly called the 'flu', is a serious disease and annual outbreaks and epidemics are caused by influenza A and B viruses. Influenza is a highly contagious viral illness and is characterised by a sudden onset of debilitating clinical symptoms which affect the entire body. Up to 500 million people are infected by influenza and up to 500,000 deaths are attributed to influenza each year. Influenza complications occur in all patient groups and include bronchitis, sinusitis, otitis media, and pneumonia.

## About Tamiflu

Tamiflu is designed to be active against all clinically relevant influenza viruses and works by blocking the action of the neuraminidase (NAI) enzyme on the surface of the virus. When neuraminidase is inhibited, the virus is not able to spread to and infect other cells in the body. It is licensed for the treatment and prophylaxis of influenza in children aged one year and above and in adults.

# Roche's efforts to support government pandemic stockpiling

The World Health Organization (WHO) advises that stockpiling antivirals in advance is presently the only way to ensure that sufficient supplies are available in the event of a pandemic. Roche has been working closely with WHO and national governments to ensure governments are aware of the importance of stockpiling antivirals in the event of a pandemic situation. Roche has received and fulfilled pandemic orders for Tamiflu from more than 75 countries worldwide. The magnitude of these orders varies with some countries, France, Finland, Iceland, Ireland, Luxembourg, Netherlands, New Zealand, Norway, Switzerland and UK stockpiling or intending to stockpile adequate Tamiflu to cover 20-40% of their population. Roche has also donated 5.125 million courses of Tamiflu treatment to the WHO for international rapid response and regional response to a pandemic influenza strain.

Roche and Gilead

Tamiflu was invented by Gilead Sciences and licensed to Roche in 1996. Roche and Gilead partnered on clinical development, with Roche leading efforts to produce, register and bring the product to the markets. Under the terms of the companies' agreement, amended in November 2005, Gilead participates with Roche in the consideration of sub-licenses for the pandemic supply of oseltamivir. To ensure broader access to Tamiflu for all patients in need, Gilead has agreed to waive its right to full royalty payments for product sold under these sub-licenses.

**About Roche** 

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As a supplier of innovative products and services for the early detection, prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2005 sales by the Pharmaceuticals Division totalled 27.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.2 billion Swiss francs. Roche employs roughly 70,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet (www.roche.com).

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Additional information

- Roche Health Kiosk, Influenza
- About Tamiflu
- About influenza
- WHO: Global influenza programme
- WHO: Avian flu

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Rache

Media Release

Basel, 2 October, 2006

Additional benefit for patients resulting from combination therapies with Roche cancer medicines

Impressive study results on Xeloda, Herceptin and Avastin presented at ESMO

Roche presented significant data on key cancer therapies at the 31<sup>th</sup> European Society for Medical Oncology (ESMO) congress, taking place in Istanbul, Turkey from September 29<sup>th</sup> until today. The many abstracts and oral presentations at the congress covered data in colorectal cancer, breast cancer and other types of the disease. Impressive data was presented on Xeloda, Avastin and Herceptin:

- Oral Xeloda combination therapy showed to be as effective as and more convenient than the current standard treatment of advanced colorectal cancer – a further proof of Xeloda's significance in various treatment regimens.
- New data underline the key role of Avastin in treating advanced (or metastatic) colorectal
  cancer Avastin plus two different oxaliplatin-based chemotherapies significantly improved
  the probability of delaying the progression of the disease compared to chemotherapy alone
- Positive results of Herceptin in combination with hormonal therapy (TANDEM study) and Xeloda (CHAT study) demonstrate the high clinical benefit of Herceptin for women with an advanced stage of HER2-positive breast cancer

Eduard Holdener, Head Global Development at Roche said:" These results are very convincing and prove that our cancer medicines can be used effectively in different combinations and at different stages of a disease. We will continue to develop the potential of our medicines and assess combination therapies to further optimise treatment options that make a real difference for patients".

Currently, up to 45,000 patients and around 7000 clinics are participating in global oncology trials managed by the Roche Group.

# Roche's presentations at ESMO

- Avastin and Xeloda: new standards for the treatment of first line metastatic colorectal cancer
   Results from an international Phase III study showed that:
  - the chemotherapy combination XELOX (oral Xeloda plus oxaliplatin) is as effective
    in terms of progression-free survival (PFS), and more convenient than the current
    standard treatment FOLFOX- 4 (infused 5-FU/leucovorin plus oxaliplatin) in the
    treatment of advanced (metastatic) colorectal cancer.
  - the addition of the anti-angiogenic agent Avastin to chemotherapy (FOLFOX-4 and XELOX) significantly improves PFS compared to chemotherapy alone.

These data are very encouraging for doctors and patients alike and further endorse that oral Xeloda should replace infused 5-FU/leucovorin in colorectal cancer regimens. When compared to the FOLFOX-4 regimen, patients on the XELOX combination have significantly more free time from infusion treatment and fewer hospital/clinic visits. In addition, the study confirms that by adding Avastin to chemotherapy can improve progression-free survival even further.

Please check <a href="http://www.roche.com/med-div-2006-10-02c.hum">http://www.roche.com/med-div-2006-10-02c.hum</a> for more information on these results.

# Herceptin: new data from two studies

The TANDEM study showed that Herceptin added to hormonal therapy increases progression-free survival in patients with advanced HER2-positive breast cancer. Adding Herceptin to the hormonal therapy, anastrozole, was shown to keep cancer under control for a significantly longer duration than hormonal therapy alone in patients whose advanced breast cancer is hormone receptor-positive, as well as HER2-positive.

Hormone receptor-positive breast cancer affects two-thirds of patients with breast cancer and is typically considered 'lower-risk' due to successful treatment with hormonal therapies. However, up to a quarter of these breast cancers are also HER2-positive. This is the first randomised study to show that this specific subset of 'co-positive' patients (both hormone receptor and HER2-positive) is actually 'higher-risk' or worse off, making these positive results highly meaningful.

For more information about the TANDEM study, please check <a href="http://www.roche.com/med-div-2006-10-02b.htm">http://www.roche.com/med-div-2006-10-02b.htm</a>

A second study, CHAT, showed that patients with HER2-positive breast cancer significantly benefit from addition of Xeloda to Herceptin and Taxotere therapy. New data presented at ESMO showed that the addition of Xeloda (capecitabine) to the combination of Herceptin (trastuzumab) and Taxotere (docetaxel) significantly increases the amount of time patients with HER2-positive advanced breast cancer have without their disease progressing. The median time to progression increased significantly from 13.8 to 18.2 months (p-value = 0.045).

These results provide the first evidence that adding a third chemotherapy to the most commonly used first-line regimen of Herceptin and taxanes provides a considerable extra benefit for patients with a particularly aggressive form of the disease. The drug combination was also generally well tolerated.

For more information about the CHAT study, please check <a href=http://www.roche.com/med-div-2006-10-02.htm</a>

#### About Roche

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#### Additional information

Roche in Oncology: www.roche.com/mboncology-a.pdf

Roche Health Kiosk: www.health-kiosk.ch/start\_krebs.htm

About ESMO: www.esmo.org/

WHO on cancer: www.who.int/topics/cancer/en/

To access video clips, in broadcast standard, free of charge, please go to: www.thenewamarket.com

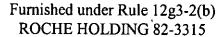
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1 P. Penault-Llorta, A. Vincent-Salomon, M. C. Mathieu, et al. On Behalf Of The Esther Study Group. Incidence and implications of HER2 and hormonal receptor overexpression in newly diagnosed metastatic breast cancer (MBC). American Society of Clinical Oncology (ASCO) Meeting Meeting Abstracts, 23: 764, 2005.



Investor Update

Roche

Basel, 2 October 2006

Tamiflu significantly reduces the risk of death from influenza New data shows treatment was associated with more than a two third reduction in deaths

Tamiflu (oseltamivir), is effective in reducing the risk of death associated with seasonal influenza in severely ill patients, according to new data presented today. Treatment of infected adults was associated with a 21 of per cent reduction in mortality. These results presented at the InterScience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco demonstrate the importance of the role of antivirals in the management of seasonal influenza and highlights the seriousness and risk of mortality associated with it.

"The neuraminidase class of antivirals were originally assessed during their clinical development for their ability to reduce influenza symptom severity and duration in healthy adults", comments Dr Allison McGeer, Primary Investigator and Microbiologist and Infectious Disease Consultant at the Department of Microbiology, Mount Sinai Hospital, Toronto Ontario, who led today's research. "This new analysis contributes to the accumulating evidence that oseltamivir also has a significant impact in preventing serious complications including death in older at-risk individuals".

The population-based surveillance study was conducted during the two consecutive influenza seasons on a total of 512 patients who were admitted to hospital for illness associated with a positive test for influenza in Ontario, Canada. Over half of patients, mainly those with underlying illness, had been previously vaccinated. 84% were treated with antibacterial agents and 32% with antivirals (3% amantadine; 97% oseltamivir) at time of admission/diagnosis. Of the total patients with influenza who required hospital admission, 67% were diagnosed with influenza with or without pneumonia, 13% with respiratory infection (e.g. acute bronchitis) and 62% with fever/viral syndrome. Of all adult patients, 6.4% patients died and these deaths were attributed to influenza. Treatment of adults with an antiviral was associated with more than a two third reduction in death from influenza.

The authors conclude that influenza remains a major cause of morbidity and mortality in patients with underlying illness, despite prior vaccination. In addition they suggest that hospitalization may be better avoided by antiviral rather than anti-bacterial therapy in patients with influenza-like illness.

## About the study

Since January 1, 2005, the Toronto Invasive Bacterial Diseases Network (TIBDN) has performed population-based surveillance for laboratory confirmed influenza associated with hospital admission in Ontario, Canada. Eligible patients were those hospitalized for illness associated with a rapid antigen test and/or culture positive for influenza are enrolled.

Allison McGeer led the TIBDN team's analysis of the clinical features and outcomes associated with the 541 cases of severe influenza associated illness identified between 1 January 2005 and 30 April.

# Toronto Invasive Bacterial Diseases Network (TIBDN)

The TIBDN is a collaboration of all hospitals, microbiology laboratories, infection control practitioners, physicians and public health units serving the population of metropolitan Toronto and Peel Region (population 3.7 million). The goal of the network is to reduce morbidity and mortality from infectious disease by using surveillance to better understand risk factors for infection, and to improve the prevention, diagnosis and treatment of serious bacterial and viral infections.

TIBDN performs population-based surveillance for selected serious bacterial and viral infections in residents of metropolitan Toronto and Peel region. The organisation also aims to leverage information from the system to advance knowledge and understanding of serious diseases: the network collaborates actively with investigators wishing to initiate population-based surveillance for new diseases and aims to provide isolates and information to investigators studying pathogenesis, illness burden, impact of vaccination or treatment programs, and antimicrobial resistance.

More information about TIBDN can be found at: http://microbiology.mtsinai.on.ca/tibdn/

#### About influenza

Influenza, commonly called the 'flu', is a serious disease and annual outbreaks and epidemics are caused by influenza A and B viruses<sup>2</sup>. Influenza is a highly contagious viral illness and is characterised by a sudden onset of debilitating clinical symptoms which affect the entire body. Up to 500 million people are infected by influenza<sup>3</sup> and up to 500,000 deaths are attributed to influenza each year<sup>4</sup>. Influenza complications occur in all patient groups and include bronchitis, sinusitis, otitis media, and pneumonia.

# About Tamiflu

Tamiflu is designed to be active against all clinically relevant influenza viruses and works by blocking the action of the neuraminidase (NAI) enzyme on the surface of the virus. When neuraminidase is inhibited, the virus is not able to spread to and infect other cells in the body.

It is licensed for the treatment and prophylaxis of influenza in children aged one year and above and in adults.

#### About Roche

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#### References:

- McGeer, A. Siddiqi, N. Green, K.A. Low, D.E., Toronto Invasive Bacterial Diseases Network (TIBDN). Outcomes of Influenza Requiring Hospital Admission in Ontario, Canada: Two Years of Surveillance. Abstract presented at the InterScience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco on 29 September 2006
- WHO checklist for influenza pandemic preparedness planning. Geneva, World Health Organization, 2005. http://www.who.int/csr/resources/publications/influenza/WHO CDS CSR GIP 2005 4/en/
- <sup>3</sup> Ghendon Y. Influenza its impact and control. World Health Stat Q 1992;45(2-3):306-311.
- <sup>4</sup> WHO Influenza Factsheet No 211, March 2003.

## Additional information:

- Roche Health Kiosk, Influenza: www.health-kiosk.ch/start\_grip.htm
- About Tamislu: www.roche.com/med mbtamislu05e.pdf
- About influenza: www.roche.com/med\_mbinfluenza05e.pdf
- WHO: Global influenza programme: www.who.int/csr/disease/influenza/en/
- WHO: Avian flu: www.who.int/mediacentre/factsheets/avian\_influenza/en/

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(Roche)

Basel, 2 October 2006

# Herceptin added to hormonal therapy increases progression-free survival in patients with advanced HER2-positive breast cancer

Data presented for the first time today at the European Society for Medical Oncology (ESMO) meeting shows that the addition of Herceptin (trastuzumab) to the hormonal therapy, anastrozole, keeps cancer under control for a significantly longer duration than hormonal therapy alone in patients whose advanced breast cancer is hormone receptor-positive, as well as HER2-positive.

Hormone receptor-positive breast cancer affects two-thirds<sup>1</sup> of patients with breast cancer and is typically considered 'lower-risk' due to successful treatment with hormonal therapies. However, up to a quarter of these breast cancers are also HER2-positive<sup>2</sup>, an aggressive form of the disease that requires special and immediate attention because the tumours are fast-growing and there is a higher likelihood of relapse. This is the first randomised study to show that this specific subset of 'co-positive' patients (both hormone receptor and HER2-positive) is actually 'higher-risk' or worse off, making these positive results highly meaningful.

The phase III study evaluated Herceptin in combination with the hormonal therapy anastrozole versus anastrozole alone as first-line therapy (or second-line hormonal therapy) in postmenopausal women with advanced (metastatic), HER2-positive and hormone receptor-positive (ER-positive and/or PR-positive) breast cancer. Median progression-free survival, the primary endpoint of the trial, was 4. 8 months for patients who received the combination compared to 2.4 months for patients who received hormonal therapy alone (p = 0.0016). Patients in the combination arm also responded significantly better to treatment (overall response rate was 20.3% versus 6.8%; p = 0.018). There was also a positive trend in median overall survival despite the fact that more than half of patients (58/104) in the hormonal therapy alone arm crossed over to receive Herceptin when their disease had progressed (28.5 months versus 23.9 months; p = 0.325).

To date, over 310,000 patients with HER2-positive breast cancer have been treated with Herceptin worldwide. Herceptin consistently benefits patients regardless of whether it is given in the early stage or advanced settings, or whether it is in combination with chemotherapy, hormonal therapy, or as a single

agent.

Roche is now working to prepare a submission of these results to regulatory authorities in the latter half of 2006.

## About the study

The TAnDEM study, conducted by Roche, is a randomised, phase III trial. Enrolment to the trial began in 2001, and 208 HER2 and hormone receptor co-positive patients were randomized at 77 centres in 22 countries across the world. Anastrozole was scheduled at a dose of 1 mg daily until progression. Herceptin was administered in 2 mg/kg weekly doses (after an initial loading dose of 4 mg/kg) until disease progression.

Overall safety data in both arms of the trial were acceptable given the known safety profile of each of the drugs in the advanced breast cancer setting. Patients in this study will continue to be followed for any side-effects.

## About breast cancer and Herceptin

Eight to nine percent of women will develop breast cancer during their lifetime, making it one of the most common types of cancer in women<sup>3</sup>. Each year more than one million new cases of breast cancer are diagnosed worldwide, with a death rate of nearly 400,000 people per year.

In HER2-positive breast cancer, increased quantities of the HER2 protein are present on the surface of the tumour cells. This is known as 'HER2-positivity'. High levels of HER2 are present in a particularly aggressive form of the disease which responds poorly to chemotherapy. Research shows that HER2-positivity affects approximately 20-30 percent of women with breast cancer<sup>4</sup>.

Herceptin is a humanised antibody, designed to target and block the function of HER2, a protein produced by a specific gene with cancer-causing potential. It has demonstrated efficacy in treating both early and advanced (metastatic) breast cancer. Given on its own as monotherapy as well as in combination with or following standard chemotherapy, Herceptin has been shown to improve response rates, disease-free survival and overall survival while maintaining quality of life in women with HER2-positive breast cancer.

Herceptin received approval for use in the European Union for advanced (metastatic) HER2-positive breast cancer in 2000 and for early HER2-positive breast cancer in 2006. In the advanced setting, Herceptin is now approved for use as a first-line therapy in combination with paclitaxel where anthracyclines are unsuitable, as first-line therapy in combination with docetaxel, and as a single agent in third-line therapy. In the early setting, Herceptin is approved for use following standard (adjuvant) chemotherapy. Herceptin is marketed in the United States by Genentech, in Japan by Chugai and internationally by Roche.

#### About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As a supplier of innovative products and services for the early detection, prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2005 sales by the Pharmaceuticals Division totalled 27.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.2 billion Swiss francs. Roche employs roughly 70,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet (<a href="www.roche.com">www.roche.com</a>).

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Roche

Basel, 2 October 2006

Avastin and Xeloda set new standards for the treatment of first line metastatic colorectal cancer

XELOX offers a new treatment option; the addition of Avastin to oxaliplatin based chemotherapy demonstrates superior progression free survival

Results from an international, phase III study presented for the first time today at the European Society for Medical Oncology (ESMO) meeting in Istanbul, show that two innovative cancer drugs, Xeloda and Avastin, are set to provide new effective treatment options for patients with advanced colorectal cancer.

# The study showed that:

- The chemotherapy combination XELOX (oral Xeloda plus oxaliplatin) is as effective in terms of
  progression-free survival, and more convenient than the current standard treatment FOLFOX- 4
  (infused 5-FU/leucovorin plus oxaliplatin) in the treatment of advanced (metastatic) colorectal
  cancer.
- The addition of the anti-angiogenic agent Avastin to chemotherapy (FOLFOX-4 and XELOX) significantly improves progression- free survival (PFS) compared to chemotherapy alone.

No new safety findings related to Avastin or Xeloda were observed in the trial. Overall survival data are still maturing. Previous Avastin studies showed both a progression-free and overall survival benefit for Avastin when combined with chemotherapy regimens compared to chemotherapy alone in the treatment of metastatic colorectal cancer<sup>1,2</sup>.

"These results demonstrate for the first time that Avastin adds clinically meaningful and statistically significant benefit in progression-free survival when combined with an oxaliplatin based chemotherapy in the 1st line treatment of metastatic colorectal cancer. In addition, the data further endorses that oral Xeloda should replace infused 5-FU/leucovorin in colorectal cancer regimens", said Ed Holdener, Head of Roche Pharma Development. "Based on these results, we plan to file a label extension for both Avastin and Xeloda with worldwide regulatory authorities."

"These results are very encouraging for doctors and patients alike. They confirm that XELOX offers an important new treatment option for metastatic colorectal cancer – one that is equally effective and more convenient than the current standard treatment. When compared to the FOLFOX-4 regimen, patients on

the XELOX combination have significantly more free time from infusion treatment, only 2 hrs versus 48 hrs and fewer hospital/clinic visits," said Professor Jim Cassidy, co-lead investigator for the study and Cancer Research UK Professor of Oncology and Chair of Medical Oncology, Beatson Oncology Centre, at the University of Glasgow, Scotland. "In addition, the study confirms that by adding Avastin to chemotherapy we can improve progression-free survival times even further."

Avastin added to chemotherapy resulted in a clinically meaningful and statistically significant improvement of 20 percent in progression- free survival. The duration of therapy with Avastin was shorter than in previously reported trials. Early Avastin discontinuation, largely unrelated to Avastin-specific toxicity occurred at a three-fold higher rate in this study compared to previous trials<sup>1,3</sup>, which may have contributed to the outcome. Further analyses are ongoing and results will be presented at upcoming scientific meetings.

In 2004, colorectal cancer was one of the leading cancers and accounted for 13 percent of all cancers in Europe<sup>4</sup>. A World Health Organization report suggested that, in 2005, 655,000 people worldwide died from colorectal cancer<sup>5</sup>.

# About the study

The NO16966 trial is a large, international, phase III trial which finally randomised 2,034 patients. It was originally planned to compare XELOX vs FOLFOX as first-line colorectal cancer treatment including 1,000 patients:

 XELOX (Xeloda plus oxaliplatin) vs FOLFOX (intravenous bolus and infusional 5-fluorouracil plus oxaliplatin)

After release of the pivotal Avastin data in colorectal cancer in 2003, the protocol was amended to investigate using a 2 by 2 factorial design:

• XELOX + placebo vs XELOX + Avastin (7.5 mg/kg q3w) vs FOLFOX + placebo vs FOLFOX + Avastin (5.0 mg/kg q2w).

The primary objective was to answer two questions: 1) whether the XELOX regimen is non-inferior to FOLFOX; 2) whether the addition of Avastin to chemotherapy improved results compared to chemotherapy alone. The secondary endpoints included overall survival, overall response rates, time to, and duration of, response and safety profile.

# Results to date show that:

- XELOX (Xeloda plus oxaliplatin) is as effective as FOLFOX (infused 5-FU plus oxaliplatin) in terms of PFS (hazard ratio: 1.05; upper limit of the 95 percent confidence interval was below the non-inferiority margin of 1.23).
- Adding Avastin to chemotherapy (FOLFOX and XELOX) significantly improved PFS compared to chemotherapy alone (hazard ratio: 0.83). This means that adding Avastin to either chemotherapy combination improves the chances of delaying progression of the disease by 20 percent.
- No unexpected safety findings were identified for either XELOX or Avastin in this study:

- Adverse events which occurred at a rate greater than 10 percent in any of the treatment arms were: diarrhoea (FOLFOX, 11.2 percent of patients; XELOX, 20.2 percent of patients), neutropenia (FOLFOX, 43.8 percent of patients, XELOX, 7.0 percent of patients) and neurosensory toxicity (FOLFOX, 16.5 percent of patients; XELOX, 17.4 percent of patients).
- The percentage of gastrointestinal perforations was 0.6 percent in the Avastin arms compared to 0.3 percent in the placebo group. Grade 3/4 arterial thromboembolic events occurred in 1.7 percent vs 1.0 percent respectively. Grade 3/4 proteinuria was reported for 0.6 percent of all patients receiving Avastin. Wound healing complications were not observed in a higher frequency than in the placebo group (0.1 vs 0.3 percent).

#### About Xeloda

Xeloda is licensed in more than 90 countries worldwide including the EU, USA, Japan, Australia and Canada and has been shown to be an effective, safe, simple and convenient oral chemotherapy in treating over 1 million patients to date.

Roche received marketing authorisation for Xeloda as a first-line monotherapy (by itself) in the treatment of metastatic colorectal cancer (colorectal cancer that has spread to other parts of the body) in most countries (including the EU and USA) in 2001. Xeloda has also been approved by the European Medicines Agency (EMEA) and U.S. Food and Drug Administration (FDA) for adjuvant (post-surgery) treatment of colon cancer in March and June 2005, respectively.

Xeloda is licensed in combination with Taxotere (docetaxel) in women with metastatic breast cancer (breast cancer that has spread to other parts of the body) and whose disease has progressed following intravenous (i.v.) chemotherapy with anthracyclines. Xeloda monotherapy is also indicated for treatment of patients with metastatic breast cancer that is resistant to other chemotherapy drugs such as paclitaxel and anthracyclines. Xeloda recently received approval in South Korea for the first-line treatment of patients with locally advanced (metastatic) pancreatic cancer, in combination with gemcitabine. Xeloda is licensed in South Korea for the first-line treatment of stomach cancer.

The most commonly reported adverse events with Xeloda include diarrhoea, abdominal pain, nausea, stomatitis and hand-foot syndrome (palmar-plantar erythrodysesthaesia).

## About Avastin

Avastin is the first treatment that inhibits angiogenesis – the growth of a network of blood vessels that supply nutrients and oxygen to cancerous tissues. Avastin targets a naturally occurring protein called Vascular Endothelial Growth Factor (VEGF), a key mediator of angiogenesis, thus choking off the blood supply that is essential for the growth of the tumour and its spread throughout the body (metastasis).

In Europe, Avastin was approved in January 2005 and in the US in February 2004 for the first-line

treatment of patients with metastatic colorectal cancer. It received another approval in the US in June 2006 as a second-line treatment for patients with metastatic colorectal cancer. The first filing for Avastin in Japan occurred in April 2006 for the treatment of metastatic colorectal cancer. Following the filings with FDA in the US, Avastin was filed with European Health Authorities in advanced breast cancer in July and in metastatic non-small cell lung cancer (NSCLC) in August.

Roche and Genentech are pursuing a comprehensive clinical programme investigating the use of Avastin in various tumour types (including colorectal, breast, lung, pancreatic cancer, ovarian cancer, renal cell carcinoma and others) and different settings (advanced and adjuvant i.e. post-operation). The total development programme is expected to include over 40,000 patients worldwide.

### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As a supplier of innovative products and services for the early detection, prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2005 sales by the Pharmaceuticals Division totalled 27.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.2 billion Swiss francs. Roche employs roughly 70,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet (<a href="www.roche.com">www.roche.com</a>).

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